



1652

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Wilson, et al.

Examiner: --

Serial No.: 09/976,800

Group: Art Unit --

Filed: October 12, 2001

Docket: M6308A-OS/OAPT (1010-16DIV)

For: CYTOCHROME P450  
MONOOXYGENASE AND  
NADPH CYTOCHROME P450 OXIDOREDUCTASE  
GENES AND PROTEINS RELATED TO THE OMEGA  
HYDROXYLASE COMPLEX OF CANDIDA  
TROPICALIS AND METHODS RELATING THERETO

Dated: November 20, 2001

Commissioner for Patents  
Washington, D.C. 20231

#3  
199  
1/24/02  
**RECEIVED**  
JAN 22 2002  
TECH CENTER 1600/2900

INFORMATION DISCLOSURE STATEMENT

Sir:

Pursuant to Applicant(s) duty of disclosure, the information listed in the attached form PTO-1449 is brought to the attention of the Examiner. Each of the items listed on the attached form PTO-1449 were either cited by or submitted to the PTO in parent Application No. 09/302,620, filed April 30, 1999. Accordingly, copies of the listed items are not being provided. The citation of the listed items is not a representation that they constitute a complete or exhaustive listing of the relevant art or that the references are prior art. The items listed are submitted in good faith, but are not intended to substitute for the Examiner's search. It is hoped, however, that in addition to apprising the Examiner of these particular items, they will assist in identifying fields of search and in making as full and complete a search as possible.

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

I hereby certify that this correspondence (and any documents referred to as enclosed) is being deposited with the United States Postal Service as first class mail, postpaid in an envelope, addressed to the: Commissioner for Patents, Washington, D.C. 20231 on November 21, 2001.

Dated: November 21, 2001

  
Jeffrey S. Steen

The filing of this information disclosure statement is not an admission that the information cited herein is, or is considered to be, material to patentability as defined in 37 C.F.R. § 1.56(b).

- ☒ [X] This information disclosure statement is being filed within three (3) months of the filing date of this application.
- ☒ [X] To the best of Applicant(s) knowledge, this information disclosure statement is being filed before the date of mailing of a first Office Action on the merits in connection with this case.
- ☒ [X] Please charge any deficiency as well as any other fee(s) which may become due under 37 C.F.R. §1.16 and/or §1.17 at any time during the pendency of this application, or credit any overpayment of such fee(s) to Deposit Account 04-1121. Also, in the event any extensions of time for responding and/or a petition under 37 C.F.R. §1.17(i)(i) are required for the pending application(s), please treat this paper as a petition to extend the time and/or enter this Information Disclosure Statement as required and charge Deposit Account No. 04-1121 therefor. **TWO (2) COPIES OF THIS SHEET ARE ENCLOSED.**

The claims of the application are believed to patentably distinguish over the prior art and to be in condition for allowance. Early and favorable consideration of this application are respectfully requested.

Respectfully submitted,



Jeffrey S. Steen  
Reg. No. 32,063  
Attorney for Applicant(s)

DILWORTH & BARRESE, LLP  
333 Earle Ovington Blvd.  
Uniondale, NY 11553  
(516) 228-8484  
JSS:mpl

Form PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
M 6308A-OS/OAPT (1010-16DIV)SERIAL NO.  
09/976,800APPLICANT  
Wilson et al.INFORMATION DISCLOSURE  
STATEMENT BY APPLICANTFILING DATE  
October 12, 2001

GROUP ART UNIT

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	5,254,466	10/19/93	Picataggio et al.			
	5,620,878	4/15/97	Picataggio et al.			
	5,648,247	7/15/97	Picataggio et al.			

## FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
					YES	NO
WO 91/14781	3 OCT 91	PCT				

## OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	Sutter et al., NADPH-Cytochrome P450 reductase (EC 1.6.2.4) (CPR)", Swissport Sequence Data Base, 1 October 1994, XP002129696 Ac P37201
	Sutter et al.; C. tropicalis NADPH-cytochrome P450 reductase gene, complete cds." EMBL Sequence Database, 21 July 1990, XP00212697, Heidelberg DE Ac M35199
	Nelson, D. R. 1996. P450 Superfamily: Update on New sequences, gene mapping, accession numbers, and nomenclature. Pharmacogenetics. 6(1):1-42
	Garfinkel, D. 1958. Studies on pig liver microsomes. I. Enzymatic and pigment composition of different microsomal fractions. Arch. Biochem. Biophys. 77:493-509
	Klaassen, C. D., M. O. Amdur, and J. Doull. 1986. Toxicology, 3rd ed. Macmillan, New York
	Omura, T., and R. Sato. 1964. The carbon-monoxide-binding pigment of liver microsomes. I. Evidence of its hemoprotein nature. J. Biol. Chem. 239:2370-2378
	Goeptar, A. R., Heleen Scheerens and Nico P.E. Vermeulen. 1995. Oxygen and Xenobiotic Reductase Activities of Cytochrome P450. Critical Reviews in Toxicology. 25(1):25-65
	Taniguchi, H., Y. Imai, and R. Sato. 1984. Role of electron transfer system in microsomal drug monooxygenase reaction catalyzed by cytochrome P450. Arch. Biochem. Biophys. 232:585
	Potter, D. W., and D. J. Reed. 1983. Involvement of FMN and phenobarbital cytochrome P450 in stimulating a one-electron reductive denitrosation of 1-(2-chloroethyl)-3-(cyclohexyl)-1-nitrosourea catalyzed by NADPH-cytochrome P450 reductase. J. Biol. Chem. 258:6906

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
M 6308A-OS/OAPT (1010-16DIV)SERIAL NO.  
09/976,800APPLICANT  
Wilson et al.FILING DATE  
October 12, 2001

GROUP ART UNIT

**RECEIVED**

JAN 22 2002

TECH CENTER 1600/2900

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
					YES	NO

## OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	Vermilion, J. L., and M. J. Coon. 1978. Identification of the high and low potential flavins of liver microsomal NADPH-cytochrome P450 reductase. J. Biol. Chem. 253:8812
	Guengerich, F. P., and M. V. Martin. 1980. Purification of cytochrome P-450, NADPH-cytochrome P-450 reductase and epoxide hydratase from a single preparation of rat liver microsomes. Arch. Biochem. Biophys. 205:365
	Ortiz de Montellano, P. R. 1986. Cytochrome P450; Structure, Mechanism and Biochemistry. Plenum Press, New York
	Kuthen, H., and V. Ulrich. 1982. Oxidase and oxygenase function of the microsomal cytochrome P450 monooxygenase system. Eur. J. Biochem. 126:583
	Poulos, T. L., and R. Raag. 1992. Cytochrome P450 crystallography, oxygen activation and electron transfer. FASEB J. 6:674
	Mukhopadhyay, C. K. a. I. B. C. 1994. NADPH initiated cytochrome P450-mediated free metal ion independent oxidative damage of microsomal proteins. Journal of Biological Chemistry. 269(18):13390-13397
	Ross, A. D., Varghese, G., Oporto, B., Carmichael, F.J., and Isreal Y. 1995. Effects of propylthiouracil treatment on NADPH-cytochrome P450 reductase levels, oxygen consumption and hydroxyl radical formation in liver microsomes from rats fed ethanol or acetone chronically. Biochemical Pharmacology. 49(7):979-989

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
M 6308A-OS/OAPT (1010-16DIV)SERIAL NO.  
09/976,800**RECEIVED**APPLICANT  
Wilson et al.

JAN 22 2002

FILING DATE  
October 12, 2001

GROUP ART UNIT

TECH CENTER 1600/2900

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO

## OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

Yamazaki, S., Nakano, N., Imai, Y., Ueng, Y.F., Guengerich, F.P., and T. Shimada. 1996. Roles of cytochrome b5 in the oxidation of testosterone and nifedipine by recombinant cytochrome P450 3A4 and by human liver microsomes. Archives of Biochemistry and Biophysics. 325(2):174-182

Gotoh, O., Tagashira, Y., Iizuka, T., and Y. Fuji-kuriyama. 1983. Structural characteristics of Cytochrome P450. Possible location of the heme-binding cysteine in determined amino acid sequences. J. Biochem. 93(807-817)

Motohashi, K., Sogawa, K., Omura, T., and Y. Fuji-kuriyama. 1987. Gene structure of human cytochrome P450 (SCC), cholesterol desmolase. J. Biochem. 101:879-997

Kalb, V. and J. Loper. 1988. Proteins from eight eukaryotic cytochrome P-450 families share a segmented region of sequence similarity. PNAS. 85:7221-7225

Kaiser, C., S. Michaelis, and A. Mitchell. 1994. Methods in Yeast Genetics. Cold Spring Harbor Laboratory Press, USA

Sambrook, J., E. Fritsch, and T. Maniatis. 1989. Molecular Cloning: A Laboratory Manual. 2nd Ed. Cold Spring Harbor Laboratory Press, USA

Boeke, J.D., LaCroute, F., and G.R. Fink. A positive selection for mutants lacking orotidine-5'-phosphate decarboxylase activity in yeast: 5-fluoro-orotic acid resistance. Mol. Gen. Genet. (1984) 197:345-346

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
M 6308A-OS/OAPT (1010-16DIV)SERIAL NO.  
09/976,800

RECEIVED

APPLICANT  
Wilson et al.

JAN 22 2002

FILING DATE  
October 12, 2001

GROUP ART UNIT

TECH CENTER 1600/2900

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO

## OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

Picataggio, S., Deanda, K., and J. Mielenz. Determination of *Candida tropicalis* Acyl Coenzyme A Oxidase Isozyme Function by Sequential Gene Disruption. 1991. Mol. and Cell. Biol. 11:4333-4339

Rohrer, T.L. and S.K. Picataggio. Targeted integrative transformation of *Candida tropicalis* by electroporation. Appl. Microbiol. Biotechnol. 1992. 36:650-654

Picataggio, S., Rohrer, T., Deanda, K., Lanning, D., Reynolds, R., Mielenz, J. And L.D. Eirich. Metabolic engineering of *Candida tropicalis* for the production of long-chain dicarboxylic acids. 1992. Bio/Technology 10:894-898

Sutter, T.R., Sangard, D. and J.C. Loper. 1990. Isolation and characterization of the alkane-inducible NADPH-cytochrome P-450 oxidoreductase gene from *Candida tropicalis*. J. Biol. Chem. 265:16428-16436

Kargel, E., Menzel, R., Honeck, H., Vogel, F., Bohmer, A. and W. Schhunk. 1996. *Candida maltosa* NADPH-cytochrome P450 reductase: cloning of a full-length cDNA, heterologous expression in *Saccharomyces cerevisiae* and function of the N-terminus region of membrane anchoring and proliferation of the endoplasmic reticulum. Yeast. 12:333-348

Ohkuma, M., Muraoka, S., Tanimoto, T., Fuji, M., Ohta, A. and Takagi, M. 1995. CYP52 (cytochrome P450alk) multigene family in *Candida maltosa*: identification and characterization of eight members. DNA and Cell Biology. 14:163-173

Seghezzi, W., Meili, C., Ruffiner, R., Kuenzi, R., Sanglard, D. and A. Fiechter. 1992. Identification and characterization of additional members of the cytochrome P450 multigene family CYP52 of *Candida tropicalis*. DNA and Cell Biology. 11:767-780

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
M 6308A-OS/OAPT (1010-16DIV)SERIAL NO.  
09/976,800

RECEIVED

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANTAPPLICANT  
Wilson et al.

JAN 22 2002

FILING DATE  
October 12, 2001

GROUP ART UNIT

TECH CENTER 1600/2900

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
					YES	NO

## OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	Sutter et al., Isolation and Characterization of the Alkane-inducible NADPH-Cytochrome P-450 Oxidoreductase Gene from <i>Candida tropicalis</i> , The Journal of Biological Chemistry, Vol. 265, 25 September 1990, pp. 16428-16436, XP000867883
	Ohkuma et al., C. Maltosa ALK2-A and ALK3-A Genes for n-alkane inducible cytochrome P-450, EMBL Sequence Database 14 March 1995, XP002139858, Heidelberg DE Ac X55881
	Ohkuma et al., Cytochrome P450 52D1, Swissprot Sequence Data Base, 15 December 1998, XP002139859, Ac Q12585
	Ohkuma, et al., CYP52 (Cytochrome P450alk) Multigene Family in <i>Candida maltosa</i> : Identification and Characterization of Eight Members, DNA and Cell Biology, Vol. 14, 1995, pp. 163-175, XP000920907
	Kobayashi et al., Quantitative Analysis of Human Multidrug Resistance 1 (MDR1) Gene Expression by Nonisotopic Competitive Reverse Transcriptase Polymerase Chain Reaction Assay, Journal of Clinical Laboratory Analysis, Vol. 11, 1997, pp. 258-266, XP000920935
	Mattes et al., Quantitative reverse transcriptase/PCR assay for the measurement of induction in cultured hepatocytes, Chemico-Biological Interactions, Vol. 107, 6 November 1997, pp. 47-61, XP000920936
	Helfrich, et al., A quantitative reverse transcriptase polymerase chain reaction-based assay to detect carcinoma cells in peripheral blood, British Journal of Cancer, Vol. 76, No. 1, July 1997, pp. 29-35, XP000920941
	Seghezzi et al., C. tropicalis CYP52A6 gene encoding cytochrome P450alk3, EMBL Sequence Database, 27 June 1992, XP002139848, Heidelberg DE, Ac Z13010

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
M 6308A-OS/OAPT (1010-16DIV)SERIAL NO.  
09/976,800**RECEIVED**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANTAPPLICANT  
Wilson et al.

JAN 22 2002

FILING DATE  
October 12, 2001

GROUP ART UNIT

TECH CENTER 1600/2900

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
						YES	NO

## OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

	Seghezzi et al., Cytochrome P450 52A6, Swissprot Sequence Data Base, 1 April 1993, XP002139849, Heidelberg DE, Ac P30608
	Seghezzi et al., Identification and Characterization of Additional Members of the Cytochrome P450 Multigene Family CYP52 of <i>Candida tropicalis</i> , DNA and Cell Biol., Vol., 11, 1992, pp. 767-780, XP000920960
	Seghezzi et al., <i>Candida Tropicalis</i> cytochrome P450alk2 and cytochrome P450alk1 genes, EMBL Sequence Database, 10 July 1991, XP002139850, Heidelberg DE, Ac M63258
	Seghezzi et al., Cytochrome P450 52A2, Swissprot Sequence Data Base, 1 April 1993, XP002139851, Ac P30607
	Seghezzi et al., Characterization of a second alkane-inducible cytochrome P450-encoding gene, CYP52A2, from <i>Candida Tropicalis</i> , Gene, Vol. 106, 1991, pp. 51-60, XP000914690
	Sanglard et al., <i>Candida tropicalis</i> alkane-inducible cytochrome P450 gene, EMBL Sequence Database, 23 November 1989, XP002139852, Heidelberg DE, Ac M24894
	Sanglard et al., Cytochrome P450 52A1, SwissProt Sequence Data Base, 1 July 1989, XP002139853, AC P10615
	Sanglard et al., Characterization of the alkane-inducible cytochrome P450 (P450alk) gene from the yeast <i>Candida tropicalis</i> : identification of a new P450 gene family, Gene, Vol. 76, No. 1, 1989, pp. 121-136, XP000914689
	Seghezzi et al., <i>C. tropicalis</i> CYP52A8 gene encoding cytochrome P450alk5, EMBL Sequence Database, 27 June 1992, XP002139854, Heidelberg DE, Ac Z13012

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



Form PTO-1449

U.S. DEPARTMENT OF COMMERCE  
PATENT AND TRADEMARK OFFICEATTY. DOCKET NO.  
M 6308A-OS/OAPT (1010-16DIV)SERIAL NO.  
09/976,800INFORMATION DISCLOSURE  
STATEMENT BY APPLICANTAPPLICANT  
Wilson et al.FILING DATE  
October 12, 2001

GROUP ART UNIT

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

## OTHER PRIOR ART (Including Author, Title, Date, Pertinent Pages, Etc.)

			Seghezzi et al., Cytochrome P450 52A8, Swissprot Sequence Data Base, 1 April 1993, XP002139855, Ac P30610
			Seghezzi et al., C. tropicalis CYP52A7 gene encoding cytochrome P450alk4, EMBL Sequence Database, 27 June 1992, XP002139856, Heidelberg DE, Ac Z13011
			Seghezzi et al., Cytochrome P450 52A7, Swissprot Sequence Database, 1 April 1993, XP002139857, Ac P30609

EXAMINER

DATE CONSIDERED

\* EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.